1: Biochem Biophys Res Commun. 1993 Mar 31;191 (3):1326-31.

ELSEVIER FULL-TEXT ARTICLE

A receptor-mediated antigen delivery and incorporation system. Administration of alpha 2-macroglobulin-cytochrome c conjugate induced high concentrations of antibodies against cytochrome c in mice.

Mitsuda S, Nakagawa T, Osada T, Ikai A.

Department of Biological Sciences, Faculty of Bioscience and Biotechnology, Tokyo Institute of Technology, Kanagawa, Japan.

Specific receptors for alpha 2-macroglobulin (alpha 2M) are found on the plasma membrane of macrophages (M phi s), one of antigen presenting cells. So far, a receptor-mediated effective uptake by M phi of foreign antigens which were linked to alpha 2M has been shown to provoke a remarkable increase in the proliferation of T lymphocytes and in the production of antibodies in vitro. Such results encouraged us to develop a new type of vaccine using a receptor-mediated antigen delivery and incorporation system based on alpha 2M and its receptor interaction. In this report, we applied the system to experimental animals. Yeast cytochrome c was used as an antigen to see if the system worked in vivo as well as in vitro. Cytochrome c was conjugated to alpha 2M through the action of trypsin and intraperitoneally administered to mice. The titer induced in mice was measured by enzyme linked immunosorbent assay (ELISA). The production of antibodies against cytochrome c was significantly increased when the protein was given in conjugated forms with alpha 2M.

PMID: 7682069 [PubMed - indexed for MEDLINE]

1: Biochem Biophys Res Commun. 1987 Jul 15;146(1):26-31.

ELSEVIER FULL-TEXT ARTICLE

Murine T cell proliferation can be specifically augmented by macrophages fed with specific antigen: alpha-2-macroglobulin conjugate.

Osada T, Noro N, Kuroda Y, Ikai A.

Foreign antigens conjugated to alpha-2-Macroglobulin (alpha-2-M) were effectively taken up by murine macrophages via alpha-2-M receptors. Such effective internalization of alpha-2-M:antigen conjugate by macrophages resulted in a remarkable increase in its ability to activate murine immune T cells under the following conditions. After macrophages were incubated with alpha-2-M:antigen conjugate or unconjugated antigen, they were cultured with immune T cells and antigen-stimulated tritiated thymidine incorporation by T cells was measured. The stimulation of T cell proliferative response by macrophages fed with the conjugate was sixteen times higher than what was observed with macrophages pretreated in the same concentration of unconjugated antigen. These findings suggest a physiological function of alpha-2-M and give us a new technique of immunization.

PMID: 2440432 [PubMed - indexed for MEDLINE]

1: Int J Cancer. 1988 Mar 15;41(3):359-63.

Tumor-associated alpha-2-macroglobulin in human melanomas.

Matoska J, Wahlstrom T, Vaheri A, Bizik J, Grofova M.

Cancer Research Institute, Bratislava, Czechoslovakia.

We and others have previously shown that human melanoma cell lines in culture synthesize alpha-2-macroglobulin (alpha 2M). We have now studied melanomas from 30 patients for the presence of alpha 2M using the peroxidase anti-peroxidase technique on histologic sections from paraffin-embedded tissues and primary antibody raised against tumor-associated alpha 2M in rabbits. alpha 2M was detected in 10 of the 30 melanomas studied. In all but 2 cases the presence of alpha 2M was restricted to solitary tumor cells or to solitary foci of tumor tissue. In one case of melanoma almost all tumor cells were positive for alpha 2M, while in the others between 20% and 50% of tumor cells were positive. In all but one of the melanomas, the positivity was characteristic of epithelioid or large-cell type or was confined to this component in melanomas with more than one cell type. In 4 positive cases, differences in the extent of alpha 2M-containing tumor tissue were observed between primary tumor and metastases or metastases from different localizations, with equivocal trend. Clinical follow-up of the melanoma patients suggested that alpha 2M-positively tends to correlate with an unfavorable prognosis.

PMID: 2450069 [PubMed - indexed for MEDLINE]

1: Int J Cancer. 1986 Jan 15;37(1):81-8. Related Articles, Links

Human tumor cells synthesize and secrete alpha-2-macroglobulin in vitro.

Bizik J, Vaheri A, Saksela O, Kalkkinen N, Meri S, Grofova M.

In previous studies we showed that human sarcoma and melanoma cell lines synthesize and secrete into culture medium a glycoprotein, migrating in urea sodium dodecyl sulfate-polyacrylamide gel electrophoresis at Mr 140,000. It is not detected in cultures of the corresponding normal cells. Conditioned medium of the melanoma cell line HMB-2, producing among the cell lines tested the largest amounts of this glycoprotein, has now been used as a source for purification of the protein. NH2-terminal amino-acid sequence determination of the purified glycoprotein showed that it is identical to human alpha 2-macroglobulin (alpha 2M). Rabbit antibodies raised against the glycoprotein specifically reacted in immunoblotting and immunodiffusion tests with alpha 2M present in human plasma. Likewise, these antibodies immunoprecipitated from the conditioned media of 35S-methionine-labelled melanoma and osteosarcoma cell lines the protein which had a molecular weight corresponding to alpha 2M. alpha 2M was also synthesized and secreted by 2 strains of fetal lung fibroblasts but not by fetal skin fibroblasts or adult skin fibroblasts autologous to the osteosarcoma cell line.

PMID: 2416700 [PubMed - indexed for MEDLINE]

1: Biochem Mol Biol Int. 1995 Nov;37(5):917-23. Related Articles, Links

Prostate specific antigen-alpha 2-macroglobulin complexes in prostate cancer patient sera.

Heeb MJ, Espana F, Gittes RF, Griffin JH.

Scripps Research Institute, La Jolla, CA 92037, USA.

Quantitative immunoblotting of prostate cancer patient sera revealed that most prostate specific antigen was in complexes with alpha 1-antichymotrypsin or alpha 2-macroglobulin with little of it being free antigen. Complexes of prostate specific antigen with these protease inhibitors in patient sera comigrated during electrophoresis with the respective purified complexes. Each complex was selectively removed from patient sera by absorption with specific antibodies. When prostate specific antigen was added to normal plasma, complexes with alpha 2-macroglobulin appeared first and after 1 hr, the distribution was approximately 40% free antigen, approximately 40% complexes with alpha 2-macroglobulin, and approximately 20% complexes with alpha 1-antichymotrypsin. These data show that prostate specific antigen reacts more readily with alpha 2-macroglobulin than with any other protease inhibitor in plasma and that the antigen complexes with alpha 2-macroglobulin in vivo in cancer patients.

PMID: 8624498 [PubMed - indexed for MEDLINE]